Remarks/Argument

Reconsideration of this application is respectfully requested. Upon entry of the amendments, claims 19-27 are pending. Claims 1-18 have been canceled herein without prejudice or disclaimer. Support for new claims 19-27 can be found throughout the specification and claims as filed. No new matter is added.

Claim Objections

Claims 1-3, 5-13, and 16-17 were objected to for general lack of clarity and for reciting non-elected subject matter. *See* Office Action at pp. 2-3. Claims 1-18 are canceled herein. Thus, the objections are moot and should be withdrawn.

New claims 19-27 are presented herewith, wherein the full name of LASP-1 is provided (*e.g.*, LIM and SH3 Domain Protein-1 (LASP-1)). Although new claims 19-27 recite sequences additional to that of the elected SEQ ID NO:13, Applicants submit that this is not improper. A close reading of the specification indicates that SEQ ID NOS:13 and 17 are smaller fragments of SEQ ID NO:1 (LASP-1) and in certain embodiments are used to perform the elected immunodiagnostic sandwich assay. Since the sandwich assay necessarily requires the use of 2 antibodies, recitation of SEQ ID NO:17 is not improper. Applicants respectfully assert that new claims 19-27 are not objectionable.

Indefiniteness

Claims 1-3, 5-13, and 16-17 were rejected under 35 USC § 112, ¶ 2 as indefinite for the reasons outlined by the Examiner. *See* Office Action at p. 3. Claims 1-18 are canceled herewith. Thus, these rejections are moot and should be withdrawn.

New claims 19-27 presented herewith do not recite the objectionable language cited by the Examiner. Thus, Applicants believe new claims 19-27 overcome the rejection.

Utility/ Enablement

Claims 1-3, 5-13, and 16-17 are rejected as unpatentable for lack of either a specific, substantial, and credible asserted utility, or a well-established utility. *See* specification at p. 7. The Examiner's position is that LASP-1 is not an effective biomarker for a particular type of disease because the specification shows it is up-regulated for more than one condition and, thus, cannot be an effective biomarker for a particular type of disease. *See id.* Claims 1-18 are canceled herewith. Thus, the rejection is moot with respect to these claims. Applicants traverse the rejections as applied to the new claims presented herewith.

Applicants respectfully assert that the claimed methods have a specific, substantial, and credible utility, and therefore are patentable under 35 U.S.C. §101. New claim 19, from which claims 20-27 directly or indirectly depend, recite a method for confirming a clinical diagnosis of a sepsis in a patient suspected of having sepsis, by determining the concentration of LIM and SH3 Domain Protein-1 (LASP-1) and at least one further biomarker for sepsis in a blood or serum sample from said patient, and comparing said concentrations to the corresponding concentration in a control sample, wherein an elevated concentration of a LASP-1 protein and at least one further biomarker for sepsis with reference to said control sample is indicative of

sepsis. Thus, the claims have been amended to clarify that the claimed invention is directed to determining the concentration of LASP-1 and at least one other sepsis biomarker. A close reading of the specification and claims presented herewith indicates that the additional determination of LASP-1 serves to confirm that the patient has sepsis.

Moreover, and as recited by the new claims, the determination of sepsis biomarkers is conducted only in those patients suspected of having sepsis. Those of ordinary skill in the art at the time of invention would have appreciated that such a suspicion would be founded on a patient's acute clinical symptoms or the patient's history (*e.g.*, a patient who underwent surgery, had an accident with a high risk of wound infection, a heavy local infection, etc.). Unlike sepsis, Alzheimer's, cardiac infarctions, and other conditions associated with increased levels of LASP-1 are not acute conditions. Thus, patients with these conditions belong to a completely different patient group and can be readily distinguished and differentiated from patients suspected of having sepsis without conducting a blood or serum assay.

Accordingly, Applicants believe these amendments and remarks address the Examiner's concerns regarding how the claimed methods can be used to differentiate between the indicated conditions. Applicants submit that the claimed methods have utility as confirmation of a diagnosis of sepsis, thus demonstrating a real world use and patentable utility. Reconsideration and withdrawal of the rejection is requested.

Claims 1-3, 5-13, and 16-17 are also rejected as unpatentable for lack of enablement. The Examiner asserts that since the claimed invention is not supported by either a specific asserted utility or a well established utility, one of ordinary skill in the art would not know how to use the claimed invention. See specification at p. 10. The Examiner further alleges that in

view of the *Wands* factors, the specification fails to teach one of ordinary skill in the art how to make and/or use the invention without undue experimentation. *See* Office Action at pages 11-14. Claims 1-18 are canceled herewith. Thus, the rejection is moot with respect to these claims. Applicants traverse the rejections as applied to the new claims presented herewith.

As indicated above, new claims 19-27 are directed to, in relevant part, methods for confirming a clinical diagnosis of a sepsis in a patient suspected of having sepsis, by determining the concentration of LIM and SH3 Domain Protein-1 (LASP-1) and at least one further biomarker for sepsis in a blood or serum sample from said patient, and comparing said concentrations to the corresponding concentration in a control sample, wherein an elevated concentration of a LASP-1 protein and at least one further biomarker for sepsis with reference to said control sample is indicative of sepsis.

Applicants contend that the new claims are enabled such that one of ordinary skill in the art would have known how to use the invention over the full scope of the claims as of the filing date of the instant application, without undue experimentation. While the *Wands* factors are instructive in evaluating whether a claimed invention is enabled, no one factor is dispositive in determining if the enablement requirement has been met. *See Enzo Biochem, Inc. v. Calgene, Inc.*, 188 F.3d 1362, 52 USPQ2d 1129, 1135-36 (Fed. Cir. 1999).

The specification clearly indicates that sepsis diagnosis is confirmed (*i.e.*, a positive result) where a patient has an elevated concentration of LASP-1 and an elevated concentration of at least one other biomarker for sepsis, as compared to the corresponding concentrations of the same sepsis biomarkers in a control sample. *See* specification at paragraphs [0034], [0039], [0043] and Fig. 4, and [0095] – [0105]. This language is also recited in the claims. For example, Figures 3 and 4 and the corresponding text at paragraphs [0104] and [0105] indicate that

compared to controls, patients having sepsis also had an increased concentration of LASP-1 in their blood or serum. Furthermore, a close reading of the specification clearly indicates which other sepsis biomarkers can be used to confirm the diagnosis. Those of ordinary skill in the art at the time of invention would have recognized that the determination of the prohormone, procalcitonin ("PCT"), is a sepsis biomarker and is also an acknowledged diagnostic sepsis test, which is currently approved by the FDA. Paragraph [0010] of the published application clearly indicates this fact and references U.S. Patent No. 5,639,617, which claims methods for early detection of a sepsis in a patient in need thereof by determining in a sample of a biological liquid of a patient the concentration of procalcitonin, such that the determined presence and amount of procalcitonin being indicative of the presence of a sepsis. The '617 patent is assigned to B.R.A.H.M.S., which is also the real party in interest in the instant application. C-reactive protein was also known to those of ordinary skill in the art at the time of invention as a biomarker for diagnosing sepsis. *See, e.g.*, Matson et al., C-reactive protein as a diagnostic test of sepsis in the critically ill, *Anaesth Intensive Care* 1991, 19:182-186. The specification further cites related applications, of which one of the Applicants is a co-inventor, for the purpose of teaching co-determination of multiple biomarkers for sepsis. *See* specification at paragraphs [0012, and 0019-0020]. Several of these related applications pertaining to further biomarkers of sepsis correspond to U.S. Patent Nos. 7,157,081; 7,153,662; 7,132,246; and 6,756,483.

It is a well-established principle in patent law that a determination of enablement must be based on the evidence as a whole. *See Wands* 858 F.2d 737, 740; 8 USPQ2d 1400, 1404, 1407 (Fed. Cir. 1988). Here, a consideration of the *Wands* factors and the evidence as a whole favor enablement of the claimed invention as amended herein. The quantity of experimentation necessary to perform the claimed invention would require no more than routine experimentation.

The state of the prior art is such that as of the filing date of the instant application those ordinarily skilled in the art (at the M.D. or Ph.D. level) would have accepted that patients suffering from sepsis present differently from patients suffering from severe inflammation disorders having other causes, and would have further recognized that determining the presence and/or concentration of a sepsis biomarker (*e.g.*, procalcitonin) is an acknowledged diagnostic sepsis test. Moreover, a plain reading of the instant specification shows that it contains sufficient guidance on:

1. identification of LASP-1 and fragments thereof (*see, e.g.*, specification at paragraphs [0055-0070];
2. how to make an immunodiagnostic determination of LASP-1 in sera of human patients (*see, e.g.*, specification at paragraphs [0072-0090];
3. how to perform the immunoassays and detect the serum concentration of LASP-1 and a further sepsis biomarker and evaluation of same [0010; 0091-0105]; and Figures 3 and 4); and
4. what constitutes a positive result – namely, a blood or serum concentration of LASP-1 in a patient who also exhibits an elevated concentration of at least one further sepsis biomarker, as compared to corresponding concentrations in a control (*see* specification at paragraphs [0104-0105] and Figures 3 and 4).

Thus, Applicants assert that the specification provides sufficient guidance reasonably correlating to the claimed methods over their full scope as amended herein. One of skill in the art at the time of invention would have accepted the disclosed model as reasonably correlating to the condition of sepsis and accepted that elevated blood or serum levels of LASP-1 and at least

one other sepsis biomarker are reasonably predictive for diagnosing same. A rigorous or an invariable exact correlation is not required. *See* MPEP § 2164.02. Reconsideration and withdrawal of the enablement rejection is respectfully requested.

Novelty

Claims 1-3, 6-7, 11-12, and 16-17 are rejected as anticipated by U.S. Patent No. 5,981,218 to Rio et al. ("Rio"). *See* Office Action at pp. 15-17. Claims 1-18 are canceled herewith. Thus, the rejection is moot with respect to these claims and should be withdrawn. Applicants traverse the rejections as applied to the new claims presented herewith.

New claim 19, from which claims 20-27 directly or indirectly depend, recites a method for confirming a clinical diagnosis of a sepsis in a patient suspected of having sepsis, by determining the concentration of LIM and SH3 Domain Protein-1 (LASP-1) and at least one further biomarker for sepsis in a blood or serum sample from said patient, and comparing said concentrations to the corresponding concentration in a control sample, wherein an elevated concentration of a LASP-1 protein and at least one further biomarker for sepsis with reference to said control sample is indicative of sepsis.

Rio does not teach the use of LASP-1 (in conjunction with at least one additional sepsis biomarker) as a biomarker for confirming a diagnosis of sepsis. Consequently, Rio cannot be interpreted to anticipate claim 19. Thus, claim 19 is novel over Rio. Similarly, claims 20-27, which depend directly or indirectly from claim 19 and, thus, necessarily incorporate all of the limitations thereof, are also novel over Rio.

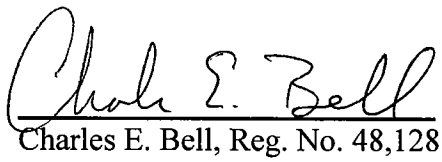
Conclusion

For all of the foregoing reasons, Applicants respectfully submit that new claims 19-27 as presented herewith are in condition for allowance. Reconsideration and withdrawal of the rejections is respectfully requested. Should any questions or issues arise concerning the application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

With a petition for three-month extension of time and payment of the corresponding fee, this Response is due on or before September 21, 2007. The Commissioner is hereby authorized to charge payment of any additional fees that may be required, or credit any overpayment of same, to Deposit Account No. 08-1935, Reference No. 2582.016.

Respectfully submitted,

Dated: September 20, 2007



Charles E. Bell, Reg. No. 48,128
Attorney for Applicants
Heslin Rothenberg Farley & Mesiti P.C.
Telephone: (518) 452-5600
Facsimile: (518) 452-5579
Customer Number 23405